Relationship between Volatile Organic Compounds (VOCs) in exhaled breath determined by Proton Transfer Reaction Time of Flight Mass Spectrometry (PTR-TOF-MS), clinical characteristics and airway inflammation in COPD

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Background
• Chronic obstructive pulmonary disease (COPD) is a heterogeneous condition.
• Breathomics presents an opportunity to phenotype this heterogeneity.
• How breath volatile organic compounds (VOCs) relate to clinical features of disease, airway physiology and inflammation is uncertain.

Methods
• Single centre prospective study; moderate to severe COPD.
• 35 COPD subjects, 379 breath samples collected using Reciva (figure 1).
• Proton Transfer Reaction-Time Flight Mass Spectrometry used (PTR-MS).
• Breathomic data analysed using PLS-DA model and receiver-operator characteristic (ROC) curves generated.
• Profiles associated with spirometry, lung volumes, gas transfer, symptoms (mMRC and CAT questionnaires), sputum eosinophils (< versus ≥1%) and neutrophils (< versus ≥61%).

Results
• Clinical characteristics were as shown Table 1.
• No distinct VOC breath profiles associated with airway physiology or symptoms.
• Sputum eosinophil and neutrophil cut-offs did identify distinct profiles with a ROC area-under-the-curve (95% confidence intervals) 0.84 (0.77-0.86) and 0.80 (0.69-0.81) respectively. Figure 2 ROC curve for sputum Neutrophils. Figure 3 ROC curve for sputum eosinophils.

Table 1: Clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>n = 80</th>
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<tbody>
<tr>
<td>Age years (range)</td>
<td>70 (66-74)</td>
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<tr>
<td>Female, n (%)</td>
<td>23 (28.75)</td>
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<tr>
<td>Caucasian, n (%)</td>
<td>80 (100)</td>
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<tr>
<td>Current smoker, n (%)</td>
<td>7 (8.75)</td>
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<td>Pack years (SD)</td>
<td>45.89 (30.09)</td>
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<tr>
<td>BMI, kg/m2 (SD)</td>
<td>27.74 (6.32)</td>
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<tr>
<td>FEV1 % predicted (SE)</td>
<td>55.00 (2.25)</td>
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<tr>
<td>Gold Stage</td>
<td></td>
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<tr>
<td>I, n (%)</td>
<td>21 (26.25)</td>
<td></td>
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<tr>
<td>II, n (%)</td>
<td>30 (27.50)</td>
<td></td>
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<tr>
<td>III, n (%)</td>
<td>22 (27.50)</td>
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</tr>
<tr>
<td>IV, n (%)</td>
<td>7 (8.75)</td>
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<tr>
<td>MRC score (SE)</td>
<td>2.6 (0.06)</td>
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<tr>
<td>SGRQ score (SE)</td>
<td>45.60 (1.21)</td>
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<tr>
<td>CAT score (SE)</td>
<td>19 (0.49)</td>
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<tr>
<td>Sputum eosinophils % (SE)</td>
<td>5.13 (0.73)</td>
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</tr>
<tr>
<td>Sputum neutrophils % (SE)</td>
<td>73.39 (1.66)</td>
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</table>

Conclusion
Machine Learning outcomes are partially able to relate VOC breath profiles to inflammation but not clinical characteristics.